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U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICE

ONLINE SEARCH REQUEST FORM

ART UNIT

Please give a detailed statement of requirements. Describe as specifically as possible the subject matter to be searched. Define any terms that may have special meaning. Give examples or relevant citations, authors, or keywords, if known.

You may include a copy of the broadest and or relevant claim(s).

***************** STAFF USE ONLY

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ONLINE TIME TOTAL TIME (in minutes)

NO. OF DATABASES

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CAS ONLINE Kal Cal Caold /

DARC/QUESTEL

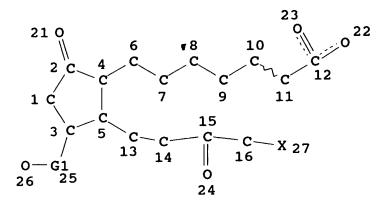
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OTHER

=> fil reg FILE 'REGISTRY' ENTERED AT 11:06:36 ON 10 DEC 92 USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT COPYRIGHT (C) 1992 American Chemical Society (ACS)

STRUCTURE FILE UPDATES: 4 DEC 92 HIGHEST RN 144785-96-6 DICTIONARY FILE UPDATES: 10 DEC 92 HIGHEST RN 144785-96-6

=> d stat que 15 L3 STR



REP G1=(0-1) C

NODE ATTRIBUTES: NONE

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 23

L5 15 SEA FILE=REGISTRY SSS FUL L3

100.0% PROCESSED 79 ITERATIONS

SEARCH TIME: 00.00.05

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L6

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(FILE 'REGISTRY' ENTERED AT 10:59:39 ON 10 DEC 92)
L5 15 S L3 FUL

15 ANSWERS

SAVE L5 GERSTL925/A

FILE 'CA' ENTERED AT 11:05:52 ON 10 DEC 92 13 S L5 OR L5/D

FILE 'CAOLD' ENTERED AT 11:06:00 ON 10 DEC 92 L7 0 S L5

FILE 'BIOSIS' ENTERED AT 11:06:14 ON 10 DEC 92 L8 0 S L5

FILE 'REGISTRY' ENTERED AT 11:06:36 ON 10 DEC 92

=> => => d ide can 15 1-15 ANSWER 1 OF 15 COPYRIGHT 1992 ACS L5 139023-32-8 REGISTRY RN Prostan-1-oic acid, 16,16-difluoro-11-hydroxy-20-methyl-9,15-dioxo-, CN methyl ester, (11.alpha.) - (9CI) (CA INDEX NAME) C22 H36 F2 O5 MF SR CA LC CA DES 4:11A.PROST

OH O
$$||$$
 CH₂-CH₂-C-CF₂-(CH₂)₄-Me O $||$ CH₂)₆-C-OMe

1 REFERENCES IN FILE CA (1967 TO DATE)

REFERENCE 1: P CA116(18):181136f

L5 ANSWER 2 OF 15 COPYRIGHT 1992 ACS
RN 138685-09-3 REGISTRY
CN Cyclopentaneheptanoic acid, 2-(4,4-difluoro-3-oxodecyl)-3-hydroxyepsilon.,5-dioxo-, 1-methylethyl ester, [1R(1.alpha.,2.beta.,3.alpha.)]- (9CI) (CA INDEX NAME)
MF C25 H40 F2 O6
SR CA
LC CA

Absolute stereochemistry.

DES

1 REFERENCES IN FILE CA (1967 TO DATE)

REFERENCE 1: P CA117(3):21186q

L5 ANSWER 3 OF 15 COPYRIGHT 1992 ACS

RN 138685-08-2 REGISTRY

CN Prostan-1-oic acid, 16,16-difluoro-11-hydroxy-6,9,15-trioxo-, 1-methylethyl ester, (11.alpha.)- (9CI) (CA INDEX NAME)

MF C23 H36 F2 06

SR CA

LC CA

DES 4:11A.PROST

1 REFERENCES IN FILE CA (1967 TO DATE)

REFERENCE 1: P CA117(3):21186q

L5 ANSWER 4 OF 15 COPYRIGHT 1992 ACS

RN 138685-07-1 REGISTRY

CN Prostan-1-oic acid, 16,16-difluoro-11-hydroxy-6,9,15-trioxo-, (11.alpha.) - (9CI) (CA INDEX NAME)

MF C20 H30 F2 06

SR CA

LC CA

DES 4:11A.PROST

OH O
$$||$$
 CH₂-CH₂-C-CF₂-Bu-n O $||$ CH₂-C-(CH₂)₄-CO₂H

1 REFERENCES IN FILE CA (1967 TO DATE)

REFERENCE 1: P CA117(3):21186q

L5 ANSWER 5 OF 15 COPYRIGHT 1992 ACS

RN 137563-84-9 REGISTRY

Prostan-1-oic acid, 16,16-difluoro-11-hydroxy-9,15-dioxo-, CN 1-methylethyl ester, (11.alpha.) - (9CI) (CA INDEX NAME) C23 H38 F2 O5 MF SR CA

LC CA

DES 4:11A.PROST

3 REFERENCES IN FILE CA (1967 TO DATE)

REFERENCE 1: P CA117(11):104249p

REFERENCE P CA116(18):181136f 2:

REFERENCE CA116(7):59071r 3: P

ANSWER 6 OF 15 COPYRIGHT 1992 ACS L5

RN 137433-40-0 REGISTRY

Prostan-1-oic acid, 16,16-difluoro-11-hydroxy-19-methyl-6,9,15-CN trioxo-, methyl ester, (11.alpha.)- (9CI) (CA INDEX NAME)

C22 H34 F2 O6 MF

SR CA

LC CA

DES 4:11A.PROST

OH O
$$\| \\ CH_2 - CH_2 - C - CF_2 - CH_2 - CH_2 - CHMe_2 \\ O O O \\ \| 0 \\ CH_2 - C - (CH_2)_4 - C - OMe \\ O$$

1 REFERENCES IN FILE CA (1967 TO DATE)

REFERENCE CA115(25):270690d 1: P

ANSWER 7 OF 15 COPYRIGHT 1992 ACS L5

RN 136790-82-4 REGISTRY

Cyclopentaneheptanoic acid, 2-(4,4-difluoro-3-oxoheptyl)-3-hydroxy-5-CN oxo-, methyl ester, [1R-(1.alpha.,2.beta.,3.alpha.)]- (9CI) (CA INDEX NAME)

MF C20 H32 F2 O5

SR CA

LC CA

DES *

Absolute stereochemistry.

2 REFERENCES IN FILE CA (1967 TO DATE)

REFERENCE 1: P CA115(19):198532j

REFERENCE 2: P CA115(19):198530g

L5 ANSWER 8 OF 15 COPYRIGHT 1992 ACS

RN 136790-80-2 REGISTRY

CN Prostan-1-oic acid, 16,16-difluoro-11-hydroxy-6,9,15-trioxo-, methyl

ester, (11.alpha.) - (9CI) (CA INDEX NAME)

MF C21 H32 F2 O6

SR CA

LC CA

DES 4:11A.PROST

OH O
$$||$$
 CH₂-CH₂-C-CF₂-Bu-n O $||$ O $||$ O $||$ CH₂-C-(CH₂)₄-C-OMe

5 REFERENCES IN FILE CA (1967 TO DATE)

REFERENCE 1: P CA117(3):21186q

REFERENCE 2: P CA116(7):59071r

REFERENCE 3: P CA115(25):270690d

CA115(19):198532j REFERENCE 4: P REFERENCE 5: P CA115(19):198530g ANSWER 9 OF 15 COPYRIGHT 1992 ACS L5 136790-76-6 REGISTRY RN Prostan-1-oic acid, 16,16-difluoro-11-hydroxy-9,15-dioxo-, CN (11.alpha.) - (9CI) (CA INDEX NAME) MF C20 H32 F2 O5 SR CA CA, CAPREVIEWS LC DES 4:11A.PROST

OH O
$$||$$
 CH₂-CH₂-C-CF₂-Bu-n O (CH₂) 6-CO₂H

6 REFERENCES IN FILE CA (1967 TO DATE)

REFERENCE 1: P CA117(11):104249p REFERENCE 2: P CA116(18):181136f REFERENCE CA116(7):59071r 3: Ρ CA115(25):270690d REFERENCE 4: P REFERENCE 5: P CA115(19):198532j REFERENCE 6: P CA115(19):198530g L5 ANSWER 10 OF 15 COPYRIGHT 1992 ACS 127545-43-1 REGISTRY RN Cyclopentaneheptanoic acid, 2-(4,4-difluoro-3-oxo-4-phenoxybutyl)-3-CN hydroxy-5-oxo-, methyl ester, [1R-(1.alpha.,2.beta.,3.alpha.)]-(9CI) (CA INDEX NAME) MF C23 H30 F2 O6

Absolute stereochemistry.

SR

LC

DES

CA

CA

1 REFERENCES IN FILE CA (1967 TO DATE)

REFERENCE 1: P CA113(3):23515n

L5 ANSWER 11 OF 15 COPYRIGHT 1992 ACS

RN 127545-41-9 REGISTRY

CN Prostan-1-oic acid, 16,16-difluoro-11-hydroxy-9,15-dioxo-, methyl

ester, (11.alpha.) - (9CI) (CA INDEX NAME)

MF C21 H34 F2 O5

SR CA

LC CA, CAPREVIEWS

DES 4:11A.PROST

8 REFERENCES IN FILE CA (1967 TO DATE)

REFERENCE 1: P CA117(11):104249p

REFERENCE 2: P CA117(3):21186q

REFERENCE 3: P CA116(18):181136f

REFERENCE 4: P CA116(7):59071r

REFERENCE 5: P CA115(25):270690d

REFERENCE 6: P CA115(19):198532j

REFERENCE 7: P CA115(19):198530g

REFERENCE 8: P CA113(3):23515n

ANSWER 12 OF 15 COPYRIGHT 1992 ACS L5

RN 127525-07-9 REGISTRY

Prostan-1-oic acid, 16-fluoro-11-hydroxy-9,15-dioxo-, (11.alpha.)-CN

(9CI) (CA INDEX NAME)

C20 H33 F O5 MF

SR CA

CA LC

DES 4:11A.PROST

4 REFERENCES IN FILE CA (1967 TO DATE)

REFERENCE 1: P CA116(7):59071r

REFERENCE 2: P CA115(25):270690d

REFERENCE CA113(9):71897k 3: P

REFERENCE 4: P CA113(1):1159x

ANSWER 13 OF 15 COPYRIGHT 1992 ACS L5

118583-22-5 REGISTRY RN

Prostan-1-oic acid, 16-fluoro-6,9,15-trioxo-11-[(tetrahydro-2H-pyran-CN

2-yl)oxy]-, ethyl ester, (11.alpha.)- (9CI) (CA INDEX NAME)

C27 H43 F 07 MF

SR CA

CA LC

DES 4:11A.PROST

1 REFERENCES IN FILE CA (1967 TO DATE)

REFERENCE 1: P CA110(19):172990d

L5 ANSWER 14 OF 15 COPYRIGHT 1992 ACS

RN 118565-87-0 REGISTRY

CN Prostan-1-oic acid, 16-fluoro-11-hydroxy-6,9,15-trioxo-,

(11.alpha.) - (9CI) (CA INDEX NAME)

MF C20 H31 F O6

SR CA

LC CA

DES 4:11A.PROST

1 REFERENCES IN FILE CA (1967 TO DATE)

REFERENCE 1: P CA110(19):172990d

L5 ANSWER 15 OF 15 COPYRIGHT 1992 ACS

RN 118565-46-1 REGISTRY

CN Prostan-1-oic acid, 16-fluoro-11-hydroxy-6,9,15-trioxo-, ethyl

ester, (11.alpha.) - (9CI) (CA INDEX NAME)

MF C22 H35 F O6

SR CA

LC CA

DES 4:11A.PROST

6 REFERENCES IN FILE CA (1967 TO DATE)

REFERENCE 1: P CA115(25):270690d

REFERENCE 2: P CA113(13):109325n

REFERENCE 3: P CA113(9):71897k

REFERENCE 4: P CA113(1):1159x REFERENCE P CA110(23):206626g 5: REFERENCE 6: Ρ CA110(19):172990d => => => fil ca FILE 'CA' ENTERED AT 11:07:52 ON 10 DEC 92 USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT COPYRIGHT (C) 1992 AMERICAN CHEMICAL SOCIETY (ACS) FILE COVERS 1967 - 28 Nov 92 (921128/ED) VOL 117 ISS 22. For OFFLINE Prints or Displays, use the ABS or ALL formats to obtain abstract graphic structures. The AB format DOES NOT display structure diagrams. => => => d bib abs hit 16 1-13 ANSWER 1 OF 13 COPYRIGHT 1992 ACS L6 AN CA117(11):104249p TI Treatment of inflammatory diseases with 15-keto-prostaglandin compounds, and preparation of and pharmaceutical compositions containing these compounds AU Ueno, Ryuji CS Kabushiki Kaisha Ueno Seiyaku Oyo Kenkyusho LO Japan SO Eur. Pat. Appl., 54 pp. PΙ EP 467564 A2 22 Jan 1992 DS R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE ΑI EP 91-306069 3 Jul 1991 PRAI JP 90-184963 10 Jul 1990 ICM A61K031-557 IC SC 1-7 (Pharmacology) SX 26, 63 DT CO **EPXXDW** PY 1992 LA Eng AN CA117(11):104249p AB 15-Ketoprostaglandin derivs. are prepd. for the manuf. of a medicament for treatment of inflammatory diseases. Thus, 13,14-dihydro-15-keto-20-ethyl-PGF2.alpha. iso-Pr ester (I) had activity against exptl. conjunctivitis in rats. An eyedrop formulation of I is given, as are injection, capsule, etc. formulations of other ketoprostaglandin derivs. Prepn. of a variety of ketoprostaglandins, e.g. 16,16-difluoro-13,14-dihydro-15-keto-PGE1 Me ester, is described. 136790-89-1 137492-12-7 137563-80-5 IT 136249-12-2 136790-88-0

```
137563-81-6 137563-84-9
                               138626-66-1
                                             140407-81-4
        (NMR spectral data for, antiinflammatory prostaglandin synthesis
        in relation to)
IT 127545-41-9P 136790-76-6P
                               136790-84-6P
                    138684-87-4P
                                   138684-93-2P
                                                  138685-02-6P
     137563-66-7P
     140407-72-3P
                    140407-76-7P
                                   140407-77-8P
                                                  140407-79-0P
     140407-80-3P
        (prepn. of, for antiinflammatory)
     ANSWER 2 OF 13 COPYRIGHT 1992 ACS
L6
AN
     CA117(3):21186q
TI
     Treatment of cataract with 15-keto-prostaglandin compounds
AU
     Ueno, Ryuji
CS
     Ueno Fine Chemical Industries, Ltd.
LO
     Japan
SO
     Eur. Pat. Appl., 43 pp.
     EP 453127 A2 23 Oct 1991
PI
        AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE
DS
ΑI
     EP 91-302925 3 Apr 1991
PRAI JP 90-90895 4 Apr 1990
     JP 90-221646 22 Aug 1990
     JP 91-29310 29 Jan 1991
IC
     ICM A61K031-557
     ICS A61K009-06
     2-9 (Mammalian Hormones)
sc
     26, 63
SX
DT
CO
     EPXXDW
PY
     1991
LA
     Eng
os
     MARPAT 117:21186
AN
     CA117(3):21186q
     15-Ketoprostaglandins are prepd. for cataract treatment. Twelve
AB
     prepn. examples are given, as are injectable, powder, capsule, and
     ophthalmic soln. formulations. The prostaglandin derivs. of the
     invention inhibited exptl. cataract in rats.
                   118696-49-4
                                 124548-58-9
                                               137563-78-1
                                                              138626-66-1
IT
     118583-21-4
   138685-08-2 138685-09-3
        (cataract treatment with)
IT 138685-07-1
        (injection soln. pharmaceutical of, for cataract treatment)
IT 136790-80-2
        (powder oral pharmaceutical of, for cataract treatment)
IT
     118565-93-8P 127545-41-9P
                                 138684-84-1P 138684-87-4P
                                   138684-98-7P
                    138684-94-3P
     138684-93-2P
                                                  138685-02-6P
     138685-06-0P
        (prepn. of, for cataract treatment)
L6
     ANSWER 3 OF 13 COPYRIGHT 1992 ACS
AN
     CA116(18):181136f
TI .
     Preparation of 15-ketoprostaglandin compounds for pharmaceuticals
     for pancreatic disease treatment
AU
     Ueno, Ryuji
```

```
CS
     Hayashibara Biochemical Laboratories, Inc.
LO
     Japan
     Eur. Pat. Appl., 35 pp. EP 455448 A2 6 Nov 1991
SO
PΙ
     R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE
DS
ΑI
     EP 91-303856 29 Apr 1991
PRAI JP 90-116139 1 May 1990
IC
     ICM A61K031-557
     63-6 (Pharmaceuticals)
SC
SX
     1, 26
DT
CO
     EPXXDW
PΥ
     1991
LA
     Eng
AN
     CA116(18):181136f
     15-Ketoprostaglandin derivs. are prepd. for manuf. of medicaments
AB
     for treatment of pancreatic disease. Prepn. of a variety of the
     derivs., e.g. 13,14-dihydro-15-keto-16,16-difluoro PGE Me ester, is
     given. Injection, oral powder, and capsule formulations are
     included. 13,14-Dihydro-15-keto-16,16-difluoro PGE2 had pancreatic
     function-improving activity in animals with exptl. acute
     pancreatitis.
                   136790-83-5 139023-32-8
IT
     120373-37-7
        (capsule pharmaceutical of, for pancreatic disease treatment)
IT 127545-41-9P 136790-76-6P
                               136790-84-6P
     137563-66-7P
        (prepn. of, for pharmaceutical, for pancreatic disease treatment)
                                  137492-12-7P
IT
     136249-12-2P 136790-89-1P
                                                   137563-80-5P
     137563-81-6P 137563-84-9P
                                  138626-66-1P 139023-34-0P
        (prepn. of, pharmacetuical compn. contg., for pancreatic disease
        treatment)
L6
     ANSWER 4 OF 13 COPYRIGHT 1992 ACS
     CA116(7):59071r
AN
TI
     Preparation and formulation of 15-ketoprostaglandins as
     cerebrovascular agents
AU
     Ueno, Ryuji; Osama, Hiroyoshi; Oda, Tomio
CS
     Kabushiki Kaisha Ueno Seiyaku Oyo Kenkyusho
LO
     Japan
SO
     Eur. Pat. Appl., 51 pp.
PΙ
     EP 435443 A2 3 Jul 1991
        AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE
DS
ΑI
     EP 90-312642
                  21 Nov 1990
PRAI JP 89-303839
                   22 Nov 1989
     JP 90-7611 17 Jan 1990
     JP 90-85439 30 Mar 1990
     ICM A61K031-557
IC
SC
     26-3 (Biomolecules and Their Synthetic Analogs)
SX
     1, 63
DT
CO
     EPXXDW
PΥ
     1991
LA
     Enq
```

ECOZR3

OH

 R^4

Title compds., e.g., I [E = CH2CH2, CH:CH; Q1 = halo; Q2 = H, halo; R1 = H, alkyl; R3 = (halo)alkyl, (alkyl)cycloalkyl, (un)substituted aryl, aryloxy; Z = bond, alkylene] were prepd. Thus, (1S,5R,6R,7R)-6-hydroxymethyl-7-tetrahydropyranyloxy-2-oxabicyclo[3.3.0]octan-3-one was oxidized and the aldehyde product condensed with (MeO)2P(O)CH2COCF2Bu to give octenylbicyclooctanone II [E = (E)-CH:CH, R = tetrahydropyranyl, R4R5 = R7R7 = O] which was converted in 3 steps to II (E = CH2CH2, R4 = R6 = OH, R5 = R7 = H). The latter was condensed with Ph3P+(CH2)4CO2H Br- and the esterified product oxidized with Collins reagent to give, after deprotection and hydrogenation, title compd. III which gave a 50% increase in blood, flow in rat hippocampus tissue 20 min after i.v. administration of 1.0 mg/kg.

IT 118583-21-4 120373-17-3 120373-24-2 122730-78-3

127525-07-9 127545-41-9 129763-67-3

131840-73-8 136249-12-2 **136790-76-6 136790-80-2**

136790-84-6 136790-88-0 137563-66-7 137563-78-1 137563-79-2

137563-80-5 137563-81-6 137563-82-7 137563-83-8

137563-84-9 137563-85-0 138626-66-1

(cerebrovascular activity of)

IT 127545-41-9P 136790-76-6P 137563-66-7P

137563-77-0P

(prepn. of, as cerebrovascular agent)

L6 ANSWER 5 OF 13 COPYRIGHT 1992 ACS

```
AN
     CA115(25):270690d
ΤI
     Treatment of hepatobiliary disease with 15-ketoprostaglandin
     derivatives
     Ueno, Ryuji; Osama, Hiroyoshi
ΑU
     Kabushiki Kaisha Ueno Seiyaku Oyo Kenkyusho
CS
LO
     Japan
SO
     Eur. Pat. Appl., 25 pp.
ΡI
     EP 424156 A2 24 Apr 1991
        AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE
DS
     EP 90-311457 18 Oct 1990
ΑI
PRAI JP 89-274606 20 Oct 1989
IC
     ICM A61K031-557
SC
     1-9 (Pharmacology)
SX
     26, 63
DT
CO
     EPXXDW
\mathbf{P}\mathbf{Y}
     1991
LA
     Eng
AN
     CA115(25):270690d
     15-Ketoprostaglandin derivs. are used to manuf. a medicament for
AB
     treatment of hepatobiliary disease. Prepn. in 8 steps of Me
     16,16-difluoro-13,14-dihydro-15-keto-PGE is described. Oral and
     injection formulations of the prostaglandin derivs. of the invention
     are given, as are animal test data.
     12619-70-4D, Cyclodextrin, di-Me ether, adduct with PGE derivs.
IT
     118565-25-6D, adduct with di-Me cyclodexrin 118565-46-1
     118565-86-9
                   120373-24-2
                                  122730-87-4 127525-07-9
     136790-89-1
                   137492-12-7
        (for hepatobiliary disease treatment)
IT
     118565-93-8
                   120373-37-7 136790-76-6 136790-80-2
   137433-40-0
        (hepatobiliary disease pharmaceutical of)
IT 127545-41-9P
        (prepn. of, for hepatobiliary disease treatment and
        pharmaceutical)
L6
     ANSWER 6 OF 13 COPYRIGHT 1992 ACS
     CA115(19):198532j
AN
     Treatment of pulmonary dysfunction with 15-keto-prostaglandin
TI
     compounds and their preparation and pharmaceutical compositions
     containing them
ΑU
     Ueno, Ryuji; Osama, Hiroyoshi
     Kabushiki Kaisha Ueno Seiyaku Oyo Kenkyusho
CS
LO
     Japan
so
     Eur. Pat. Appl., 23 pp.
ΡI
     EP 430552 A2 5 Jun 1991
         AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE
DS
ΑI
     EP 90-312641 21 Nov 1990
PRAI JP 89-303841 22 Nov 1989
IC
     ICM A61K031-557
SC
     1-9 (Pharmacology)
SX
     26, 63
DT
```

```
CO
     EPXXDW
PY
     1991
LA
     Enq
AN
     CA115(19):198532j
     15-Ketoprostaglandins are used for the manuf. of a medicament for
AB
     treatment of a pulmonary dysfunction. Prepn. of 16,16-difluoro-13,14-
     dihydro-15-keto PGE1 (I) and of I Me ester are given, as is an injection formulation contg. I. Effectiveness of the
     ketoprostaglandins of the invention was detd. in animal testing.
     Prepn. and formulations for ketoprostaglandins other than I are also
     included.
IT 127545-41-9P 136790-76-6P
        (prepn. of, for pulmonary pharmaceutical)
                   118565-93-8 136790-80-2
IT
                                               136790-81-3
     118565-26-7
                 136790-83-5
   136790-82-4
        (pulmonary pharmaceutical of)
     ANSWER 7 OF 13 COPYRIGHT 1992 ACS
L6
     CA115(19):198530g
AN
     Treatment of cardiac dysfunction with 15-keto-prostaglandin
ΤI
     compounds and their preparation and pharmaceutical compositions
     containing them
AU
     Ueno, Ryuji; Osama, Hiroyoshi
CS
     Kabushiki Kaisha Ueno Seiyaku Oyo Kenkyusho
LO
     Japan
SO
     Eur. Pat. Appl., 21 pp.
PΙ
     EP 430551 A2 5 Jun 1991
         AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE
DS
     EP 90-312640
AΙ
                   21 Nov 1990
PRAI JP 89-303840
                   22 Nov 1989
IC
     ICM A61K031-557
SC
     1-8 (Pharmacology)
     26, 63
SX
DT
CO
     EPXXDW
PΥ
     1991
LA
     Eng
AN
     CA115(19):198530q
     15-Ketoprostaglandins are used for the manuf. of a medicament for
AB
     treatment of cardiac dysfunction. Thus, 13,14-dihydro-15-keto-16,16-
     difluoro PGE1 (I) (prepn. given) increased contraction of guinea pig
     heart atria, compared to controls receiving vehicle alone. An
     injection formulation contq. I is given. Other ketoprostaglandins
     are prepd. and tested and formulations given.
IT
     118565-26-7
                    118565-93-8 136790-80-2
                                               136790-81-3
   136790-82-4
                 136790-83-5
        (cardiac pharmaceutical of)
IT 127545-41-9P 136790-76-6P
        (prepn. of, for cardiac pharmaceutical)
L6
     ANSWER 8 OF 13 COPYRIGHT 1992 ACS
AN
     CA113(13):109325n
ΤI
     15-Keto-prostaglandin E ester hypersphyxia causing composition
```

```
AU
     Ueno, Ryuzo; Ueno, Ryuji; Oda, Tomio
CS
     Kabushiki Kaisha Ueno Seiyaku Oyo Kenkyusho
LO
     Japan
SO
     Eur. Pat. Appl., 26 pp.
PΙ
     EP 343904 A1 29 Nov 1989
DS
         AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE
AΙ
     EP 89-305163
                   22 May 1989
PRAI JP 88-125303
                   23 May 1988
                   20 Jul 1988
     JP 88-182281
     ICM A61K031-557
IC
SC
     1-8 (Pharmacology)
SX
     2, 63
DT
CO
     EPXXDW
PΥ
     1989
LA
     Eng
os
     MARPAT 113:109325
AN
     CA113(13):109325n
AB
     15-Keto-PGEs ester compns. cause hypersphyxia, effective in
     recovering blood pressure and heart rate in, e.g., hemorrhage shock
     or hyperventilation. I.v. injection in rats of a no. of 14-keto-PGE
     esters exhibit a blood pressure increasing effect instead of a
     decreasing effect shown with other prostaglandins. The esters also
     exhibit pos. chronotropic effects. Examples of pharmaceuticals
     contg. the compds. are given.
ΙT
     363-23-5, 13,14-Dihydro-15-keto-PGE2
                                             5094-14-4,
                                  93036-49-8, 13,14-Dihydro-6,15-diketo-
     13,14-Dihydro-15-keto-PGE1
                                        118565-25-6, 13,14-Dihydro-6,15-
     PGE1
            118565-22-3
                          118565-24-5
     diketo-19-methyl-PGE1 ethyl ester
                                         118565-26-7,
     13,14-Dihydro-6,15-diketo-19-methyl-PGE1 methyl ester
                                                              118565-27-8
                   118565-31-4, 13,14-Dihydro-15-keto-PGE2 ethyl ester
     118565-28-9
     118565-33-6, 13,14-Dihydro-15-keto-PGE2 methyl ester
                                                             118565-34-7,
     13,14-Dihydro-15-keto-PGE2 n-propyl ester
                                                  118565-37-0
                                 118565-43-8 118565-46-1
                   118565-42-7
     118565-38-1
                   118565-63-2, (.+-.) 13,14-Dihydro-6,15-diketo-PGE1
     118565-58-5
                   118565-64-3, 13,14-Dihydro-6,15-diketo-PGE1 methyl
     ethyl ester
             118565-66-5
                           118565-69-8
                                         118565-77-8,
     13,14-Dihydro-6,15-diketo-PGE1 ethyl ester
                                                   118565-86-9
     118583-21-4
                   118583-25-8
                                 118583-32-7
                                                118583-41-8
                                                              118583-48-5
     118583-49-6
                   118628-13-0
                                 118696-35-8
                                                118696-39-2,
     13,14-Dihydro-6,15-diketo-PGE1 n-butyl ester
                                                     118696-42-7,
     13,14-Dihydro-15-keto-PGE2 n-butyl ester
                                                 118696-46-1,
     13,14-Dihydro-15-keto-PGE2 benzyl ester
                                                118696-48-3
                                                              118696-49-4
     118696-50-7
                   118696-51-8
                                 118696-52-9
                                                118696-59-6
                                                              118696-60-9,
     13,14-Dihydro-15-keto-20-ethyl-PGE2 ethyl ester
                                                        118696-61-0,
     13,14-Dihydro-15-keto-20-ethyl-PGE1 methyl ester
                                                         118696-62-1
     118696-63-2
                   118696-70-1
                                 118696-72-3, 13,14-Dihydro-6,15-diketo-
     16,16-dimethyl-PGE1 ethyl ester
                                       118720-65-3
                                                      120414-35-9,
     13,14-Dihydro-15-keto-PGE2 hydroxyethyl ester
                                                      120414-36-0
     120414-37-1
                   120414-38-2
                                 120414-45-1
                                                120445-09-2
                                                              120445-10-5,
     13,14-Dihydro-15-keto-.DELTA.2-PGE2-methyl ester
                                                         124600-33-5
     128678-58-0
                   129041-43-6
        (hypersphyxia activity of, for pharmaceuticals)
```

```
ANSWER 9 OF 13 COPYRIGHT 1992 ACS
L6
AN
     CA113(9):71897k
     15-Ketoprostaglandin E derivatives as bronchodilators
TI
AU
     Ueno, Ryuzo; Ueno, Takashi; Oda, Tomio
CS
     Kabushiki Kaisha Ueno Seiyaku Oyo Kenkyusho
LO
     Japan
SO
     Jpn. Kokai Tokkyo Koho, 23 pp.
     JP 01287028 A2 17 Nov 1989 Heisei
PΙ
     JP 88-115409 11 May 1988
AΙ
     ICM A61K031-557
IC
     2-4 (Mammalian Hormones)
SC
DT
CO
     JKXXAF
PY
     1989
LA
     Japan
AN
     CA113(9):71897k
AB
     15-Ketoprostaglandin E derivs. are bronchodilators. The
     bronchodilating activities (IC20 and IC50 values) of 64 derivs. of
     15-ketoprostaglandin E were studied in vitro using bronchial smooth
     muscle isolated from the guinea pig. The IC20 and IC50 of
     13,14-dihydro-15-keto-PGE were 8 .times. 10-7 and 7 .times. 10-6M,
                                       5094-14-4
                                                   26441-05-4
IT
     363-23-5
                363-24-6
                           745-65-3
     118565-22-3
                   118565-24-5
                                  118565-25-6
                                                118565-26-7
                                                              118565-27-8
     118565-28-9
                   118565-31-4
                                  118565-33-6
                                                118565-34-7
                                                              118565-35-8
                                  118565-42-7
                                                118565-43-8
     118565-37-0
                   118565-38-1
                               118565-64-3
                                              118565-66-5
   118565-46-1
                 118565-58-5
     118565-69-8
                   118565-77-8
                                  118565-86-9
                                                118565-94-9
                                                              118565-95-0
                                  118583-49-6
                                                118628-13-0
                                                              118696-35-8
     118583-32-7
                   118583-40-7
     118696-36-9
                   118696-39-2
                                 118696-42-7
                                                118696-46-1
                                                              118696-48-3
                                                              118696-58-5
                   118696-50-7
                                  118696-51-8
                                                118696-52-9
     118696-49-4
                                 118696-72-3
                                                118696-73-4
                                                              120414-35-9
     118696-59-6
                   118696-70-1
                                                              120445-10-5
     120414-37-1
                   120414-38-2
                                  120414-45-1
                                                120445-09-2
     124600-33-5 127525-07-9
                               128678-52-4
                                              128678-53-5
                   128678-55-7
                                 128678-57-9
                                                128678-58-0
                                                              128678-59-1
     128678-54-6
     128695-96-5
        (bronchodilator activity of)
L6
     ANSWER 10 OF 13
                     COPYRIGHT 1992 ACS
AN
     CA113(3):23515n
ΤI
     16,16-Difluoro-15-oxo-15-deoxyprostaglandin E derivatives as ulcer
     inhibitors
ΑU
     Wakatsuka, Hirohisa; Okegawa, Tadao
CS
     Ono Pharmaceutical Co., Ltd.
LO
     Japan
SO
     Jpn. Kokai Tokkyo Koho, 9 pp.
     JP 02032055 A2 1 Feb 1990 Heisei
PΙ
AΙ
     JP 88-178015
                   19 Jul 1988
IC
     ICM
          C07C405-00
     ICS
          A61K031-557
SC
     26-3 (Biomolecules and Their Synthetic Analogs)
SX
```

DT P
CO JKXXAF
PY 1990
LA Japan
OS MARPAT 113:23515
AN CA113(3):23515n
GI

HO
$$R^{2}R^{3}$$

The title derivs. I [R1 = H, C1-8 alkyl; R2 = direct bond, C1-4 AB alkylene; R3 = C1-8 alkyl, (C1-8 alkyl) C4-7 cycloalkyl, Ph or OPh which may have 1 Cl, CF3, or C1-4 alkyl; A = CH2CH2, cis-CH:CH; B = CH2CH2, trans-CH:CH; B = CH2CH2 when A = cis-CH:CH], their cyclodextrin inclusion compds., or nontoxic salts of I (R1 = H), useful as strong ulcer inhibitors with weak antihypertensive, diuretic, blood platelet aggregation-inhibiting, bronchodilatory activities, etc. common to prostaglandins, are prepd. A mixt. of 157 mg 11-(tetrahydropyran-2-yl) ether of I (R1 = Me, R2R3 = Bu, A = CH2CH2, B = trans-CH:CH), AcOH, H2O, and THF was stirred at 45.degree. for 2 h to give 113 mg I (R1 = Me, R2R3 = Bu, A = CH2CH2, B = trans-CH:CH), 38 mg of which in AcOEt was treated with Pd/C under H at room temp. for 20 min to give 34 mg I (R1 = Me, R2R3 = Bu, A = B = CH2CH2) (II). II inhibited pentagastrin-induced increase of qastric secretion in rats at ED50 <30 .mu.q/kq/h.

Ι

IT 127545-40-8P 127545-41-9P 127545-42-0P 127545-43-1P

(prepn. of, as ulcer inhibitor)

L6 ANSWER 11 OF 13 COPYRIGHT 1992 ACS

AN CA113(1):1159x

TI Use of 15-ketoprostaglandin E or F compounds for uterine contraction

AU Ryuzo, Ueno; Ryuji, Ueno; Tomio, Oda

CS Kabushiki Kaisha Ueno Seiyaku Oyo Kenkyusho

LO Japan

SO Eur. Pat. Appl., 33 pp.

PI EP 342003 A1 15 Nov 1989

DS R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE

AI EP 89-304724 10 May 1989

PRAI JP 88-115408 11 May 1988

```
JP 88-137666 2 Jun 1988
IC
     ICM A61K031-557
     2-3 (Mammalian Hormones)
SC
SX
     26, 63
DT
     P
CO
     EPXXDW
PY
     1989
LA
     Eng
os
     MARPAT 113:1159
AN
     CA113(1):1159x
     Prostanoic acid derivs. for manuf. of medicaments to induce uterine
AB
     contraction and interrupt pregnancy are selected from
     15-ketoprostaglandin E compds. (15-keto PGE) and
     15-ketoprostaglandin F compds. (15-keto PGF) with the proviso that
     when the only group, which is unsubstituted n-pentyl, is attached to
     C15 of the prostanoic acid nucleus and the bond between C5 and C6 is
     a double bond, than the bond between C13 and C14 is a single bond.
     13,14-Dihydro-15-keto-16-desbutyl-16-m-trifluoromethylphenoxy-PGE2
     was synthesized from trifluorocresol in 17 steps.
     13,14-Dihydro-15-keto-PGF2.alpha. Me ester at 3 .times. 10-5 M
     induced uterine contractions 98% that of oxytocin (1 mU).
     Formulations of 13,14-dihydro-15-keto-16-desbutyl-16-m-
     trifluoromethylphenoxy-PGF2.alpha. are given.
IT
     363-23-5
                363-24-6, PGE2
                                 551-11-1, PGF2.alpha.
                                                          27376-76-7
     31753-17-0, PGE2 methyl ester
                                      118565-25-6
                                                    118565-26-7
     118565-27-8
                   118565-28-9
                                 118565-31-4
                                                118565-33-6
                                                              118565-37-0
                                 118565-43-8 118565-46-1
     118565-38-1
                   118565-42-7
                   118565-63-2
                                 118565-66-5
                                                118565-77-8
                                                              118565-86-9
     118565-58-5
     118565-93-8
                   118565-94-9
                                 118565-95-0
                                                118583-21-4
                                                              118583-32-7
     118583-40-7
                   118583-41-8
                                 118583-49-6
                                                118594-28-8
                                                              118628-13-0
     118696-35-8
                   118696-39-2
                                 118696-49-4
                                                118696-60-9
                                                              118696-62-1
                   118696-70-1
                                 118696-72-3
     118696-63-2
                                                118720-65-3
                                                              120373-16-2
     120373-17-3
                   120373-19-5
                                 120373-20-8
                                                120373-21-9
                                                              120373-23-1
                                                120373-27-5
     120373-24-2
                   120373-25-3
                                 120373-26-4
                                                              120373-28-6
     120373-29-7
                   120373-30-0
                                 120373-31-1
                                                120373-32-2
                                                              120373-33-3
     120373-34-4
                   120373-35-5
                                 120373-36-6
                                                120373-37-7
                                                              120373-38-8
     120373-40-2
                                 120442-68-4
                   120414-38-2
                                                122730-78-3
                                                              122730-84-1
     122730-87-4
                   127525-06-8 127525-07-9
                                              127525-08-0
     127525-09-1
        (uterine contraction by)
     ANSWER 12 OF 13 COPYRIGHT 1992 ACS
L6
AN
     CA110(23):206626q
ΤI
     Fervescence composition comprising 15-ketoprostaglandins E
AU
     Ueno, Ryuzo; Ueno, Ryuji; Oda, Tomio
CS
     Kabushiki Kaisha Ueno Seiyaku Oyo Kenkyujo
LO
     Japan
SO
     Eur. Pat. Appl., 30 pp.
PΙ
     EP 292177 A1
                    23 Nov 1988
DS
         AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE
ΑI
     EP 88-304206
                   10 May 1988
PRAI JP 87-119367
                   15 May 1987
     JP 87-235962
                   17 Sep 1987
```

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IC
     ICM A61K031-557
SC
     2-9 (Mammalian Hormones)
SX
     1
DT
     P
CO
     EPXXDW
PY
     1988
LA
     Eng
     MARPAT 110:206626
os
AN
     CA110(23):206626g
GI
```

AB The 15-keto prostaglandins E [I; R = OH, hydroxyalkyl, alkyl; Y = (un)substituted hydrocarbon moiety; Z = hydrocarbon moiety] and I salts are fervescence agents. I.p. administration of 400 ng 13,14-dihydro-15-keto-PGE2 increased by 0.7.degree. the body temp. of the rat.

```
IT
     363-23-5
                363-24-6
                            745-65-3
                                       5094-14-4
                                                    31753-17-0
                                                                  93036-49-8
                                                               118565-27-8
     118565-22-3
                   118565-24-5
                                  118565-25-6
                                                 118565-26-7
                                                 118565-34-7
                                                                118565-37-0
     118565-28-9
                   118565-31-4
                                  118565-33-6
                   118565-42-7
                                  118565-43-8 118565-46-1
     118565-38-1
                   118565-63-2
                                  118565-64-3
                                                 118565-66-5
                                                               118565-69-8
     118565-58-5
                                                 118583-32-7
                                                               118583-40-7
     118565-77-8
                   118565-86-9
                                  118565-95-0
                   118583-48-5
                                  118583-49-6
                                                 118628-13-0
                                                               118696-35-8
     118583-41-8
     118696-36-9
                   118696-39-2
                                  118696-42-7
                                                 118696-46-1
                                                               118696-48-3
                   118696-50-7
                                  118696-51-8
                                                 118696-52-9
                                                               118696-59-6
     118696-49-4
                   118696-61-0
                                  118696-63-2
                                                 118696-70-1
                                                               118696-72-3
     118696-60-9
                                                 120414-37-1
                                                               120414-38-2
     118720-65-3
                   120414-35-9
                                  120414-36-0
     120414-45-1
                   120445-09-2
                                  120445-10-5
        (as fervescence agent)
```

L6 ANSWER 13 OF 13 COPYRIGHT 1992 ACS

AN CA110(19):172990d

TI Prostaglandins E and antiulcer containing compositions containing same

AU Ueno, Ryuzo; Ueno, Ryuji; Kato, Ichie; Oda, Tomio

CS Ueno Fine Chemical Industries, Ltd.

LO Japan

SO Eur. Pat. Appl., 136 pp.

PI EP 284180 A1 28 Sep 1988

DS R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE

AI EP 88-300709 28 Jan 1988

PRAI JP 87-18820 28 Jan 1987

JP 87-65352 18 Mar 1987

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IC
     ICM
          C07C177-00
     ICS
          A61K031-557
     26-3 (Biomolecules and Their Synthetic Analogs)
SC
SX
     1
DT
     P
CO
     EPXXDW
PY
     1988
LA
     Eng
os
     MARPAT 110:172990
     CA110(19):172990d
AN
GI
```

Prostaglandins E [I; X = (CH2)3, CH2COCH2, CH2CH:CH2, CH2C.tplbond.C; R1 = H, physiol. acceptable cation or protective group, alkyl, PhCH2, hydroxyalkyl; R2 = H, Me; R3 = OH, Me, CH2OH; R4, R5 = H, Me, OH, halo; R6 = alkoxy (un)substituted alkyl, alkenyl; C2-C3 may be double bond; if R1, R2, R4, R5 = H, R6 = Bu, R3 = OH], useful as antiulcer agents without uterine or intestinal constriction or vasodilation, were prepd. PGE1 deriv. II was prepd. in 13 steps from (-)-Corey lactone, Collins oxidn. of which gave an aldehyde which reacted with NaH-treated di-Me (2-oxoheptyl)phosphonate. 13,14-Dihydro-15-oxo-PGE2 Et ester had an ulcer inhibiting ED50 of 1.5 mg/kg in rats, with no intestinal or uterus constricting effects or tracheal relaxation effect; PGE2 with ulcer inhibiting ED50 of 0.5 mg/kg showed intestinal and uterus constriction as well as tracheal relaxation.

II

Ι

IT 118583-18-9P 118583-19-0P 118583-20-3P **118583-22-5P**(prepn. and reaction of, in prepn. of antiulcer prostaglandins)
IT 118565-22-3P 118565-24-5P 118565-25-6P 118565-26-7P

```
118565-27-8P
                    118565-28-9P
                                    118565-31-4P
                                                   118565-33-6P
                                    118565-37-0P
                                                   118565-38-1P
     118565-34-7P
                    118565-35-8P
                    118565-43-8P 118565-46-1P
                                                 118565-58-5P
     118565-42-7P
                                                   118565-69-8P
     118565-63-2P
                    118565-64-3P
                                    118565-66-5P
     118565-77-8P
                    118565-86-9P
                                    118583-14-5P
                                                   118583-21-4P
     118583-25-8P
                    118583-26-9P
                                    118583-32-7P
                                                   118583-34-9P
     118583-40-7P
                    118583-41-8P
                                    118583-48-5P
                                                   118583-49-6P
                                                   118628-91-4P
     118607-61-7P
                    118628-13-0P
                                    118628-14-1P
     118696-35-8P
                    118696-36-9P
                                    118696-39-2P
                                                   118696-42-7P
     118696-44-9P
                    118696-46-1P
                                    118696-48-3P
                                                   118696-49-4P
                                    118696-52-9P
                                                   118696-54-1P
     118696-50-7P
                    118696-51-8P
                                                   118696-60-9P
     118696-57-4P
                    118696-58-5P
                                    118696-59-6P
     118696-61-0P
                    118696-62-1P
                                    118696-63-2P
                                                   118696-70-1P
                    118696-73-4P
                                    118720-65-3P
     118696-72-3P
        (prepn. of, as antiulcer agent)
IT
                                    118565-86-9P 118565-87-0P
     118565-84-7P
                    118565-85-8P
                                    118565-90-5P
                                                   118565-91-6P
     118565-88-1P
                    118565-89-2P
     118565-92-7P
                    118565-93-8P
                                    118565-94-9P
                                                   118565-95-0P
     118565-96-1P
                    118565-97-2P
        (prepn. of, as ulcer inhibitor)
=> d his 19-
     (FILE 'REGISTRY' ENTERED AT 11:06:36 ON 10 DEC 92)
     FILE 'CA' ENTERED AT 11:07:52 ON 10 DEC 92
     FILE 'CAPREVIEWS' ENTERED AT 11:10:00 ON 10 DEC 92
L9
              1 S L5
=> d all
     ANSWER 1 OF 1 COPYRIGHT 1992 ACS
L9
     92:441791 CApreviews
AN
TI
     15-ketoprostaglandins or memory improver
AU
     Ueno, Takashi; Nagama, Hiroyoshi
CS
     Ueno Seiyaku Oyo Kenkyusho K. K.
LO
     Japan
SO
     Jpn. Kokai Tokkyo Koho, 11 pp.
     JP 04187637 A2 6 Jul 1992 Heisei
PΙ
     JP 90-319576 21 Nov 1990
AΙ
IC
     ICM A61K031-557
SC
     63 (Pharmaceuticals)
DT
CO
     JKXXAF
PY
     1992
LA
     Japan
AB
     15-ketoprostaglandins such as 13,14-dihydro-15-keto-16,16-
     difluoroprostaglandin E2 (I) are memory improver.
                                                         I (1-100
     .mu.g/kg) administered s.c. to exptl. mice improved the memory as
     refluxed by the passive avoidance learning behavior. Formulations
     and prepn. of 15-ketoprostaglandins are presented.
     RN LIST MAY NOT BE COMPLETE: 32233-41-3; 69222-61-3;
IT
                                                             118408-95-0;
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118565-93-8; 118583-12-3; 118583-13-4; 118583-21-4; 127545-41-9; 136790-72-2; 136790-73-3; 136790-74-4; 136790-75-5; 136790-76-6; 136790-89-1